

# Contents of Volume 47

July 1990

## Editorial

- Invited Editorial: Predictive Testing for Adult-Onset Genetic Disease: Ethical and Legal Implications of the Use of Linkage Analysis for Huntington Disease**  
Marguerite Chapman 1

## Original Articles

### Ethical and Legal Dilemmas Arising during Predictive Testing for Adult-Onset Disease: The Experience of Huntington Disease

- Marlene Huggins, Maurice Bloch, Shelin Kanani, Oliver W. J. Quarrell, Jane Theilmann, Amy Hedrick, Bernard Dickens, Abbyann Lynch, and Michael Hayden 4

### Nance-Horan Syndrome: Localization within the Region Xp21.1-Xp22.3 by Linkage Analysis

- Dwight Stambolian, Richard Alan Lewis, Kenneth Buetow, Anna Bond, and Robert Nussbaum 13

### Genetic Mapping of X-linked Albinism-Deafness Syndrome (ADFN) to Xq26.3-q27.1

- Yosef Shiloh, Gilad Litvak, Yael Ziv, Thomas Lehner, Lodewijk Sandkuyl, Minka Hildesheimer, Vered Buchris, Frans P. M. Cremers, Paul Szabo, Bradley N. White, Jeanette J. A. Holden, and Jurg Ott 20

### Mapping Autosomal Recessive Vitamin D Dependency Type 1 to Chromosome 12q14 by Linkage Analysis

- Malgorzata Labuda, Kenneth Morgan, and Francis H. Glorieux 28

### Krabbe Disease Locus Mapped to Chromosome 14 by Genetic Linkage

- Joel Zlotogora, Sulagna Chakraborty, Robert G. Knowlton, and David A. Wenger 37

### T-Cell Receptor Genes and Insulin-dependent Diabetes Mellitus (IDDM): No Evidence for Linkage from Affected Sib Pairs

- Patrick Concannon, Jocynnda A. Wright, Lawrence G. Wright, Daniel R. Sylvester, and Richard S. Spielman 45

### Genetic Counseling in Rare Syndromes: A Resampling Method for Determining an Approximate Confidence Interval for Gene Location with Linkage Data from a Single Pedigree

- Graeme K. Suthers and Sue R. Wilson 53

### Cloning and Chromosomal Localization of the Human Cytoskeletal $\alpha$ -Actinin Gene Reveals Linkage to the $\beta$ -Spectrin Gene

- Hagop Youssoufian, Marybeth McAfee, and David J. Kwiatkowski 62

### Extensive Genetic Heterogeneity in Patients with Acid Alpha Glucosidase Deficiency as Detected by Abnormalities of DNA and mRNA

- Frank Martiniuk, Mark Mehler, Stephanie Tzall, Gary Meredith, and Rochelle Hirschhorn 73

### Complex Alleles of the Acid $\beta$ -Glucosidase Gene in Gaucher Disease

- Theresa Latham, Gregory A. Grabowski, Bimal D. M. Theophilus, and Frances I. Smith 79

### Mitochondrial DNA Polymorphism Reveals Hidden Heterogeneity within Some Asian Populations

- Ranajit Chakraborty 87

### Segregation of Mitochondrial Genomes in a Heteroplasmic Lineage with Leber Hereditary Optic Neuropathy

- Johanna Vilkkki, Marja-Liisa Savontaus, and Eeva K. Nikoskelainen 95

### Partial Aldolase B Gene Deletions in Hereditary Fructose Intolerance

- N. C. P. Cross and T. M. Cox 101

### Lipoprotein Lipase Deficiency Resulting from a Nonsense Mutation in Exon 3 of the Lipoprotein Lipase Gene

- Mitsuru Emi, Akira Hata, Margaret Robertson, Per-Henrik Iverius, Robert Hegele, and Jean-Marc Lalouel 107

**Inheritance of an RNA Splicing Mutation ( $G^{+1} IVS20$ ) in the Type III Procollagen Gene (COL3A1) in a Family Having Aortic Aneurysms and Easy Bruisability: Phenotypic Overlap between Familial Arterial Aneurysms and Ehlers-Danlos Syndrome Type IV**

Sirpa Kontusaari, Gerard Tromp, Helena Kuivaniemi, Roger L. Ladda, and Darwin J. Prockop 112

**Human Serum Deoxyribonuclease I (DNase I) Polymorphism: Pattern Similarities among Isozymes from Serum, Urine, Kidney, Liver, and Pancreas**

Koichiro Kishi, Toshihiro Yasuda, Yoko Ikehara, Kazumi Sawazaki, Wataru Sato, and Reiko Iida 121

**A Homozygous Transthyretin Variant Associated with Senile Systemic Amyloidosis: Evidence for a Late-Onset Disease of Genetic Etiology**

Daniel R. Jacobson, Peter D. Gorevic, and Joel N. Buxbaum 127

**Age at Menarche as a Fitness Trait: Nonadditive Genetic Variance Detected in a Large Twin Sample**

Susan A. Treloar and Nicholas G. Martin 137

**Angelman Syndrome: Three Molecular Classes Identified with Chromosome 15q11q13-specific DNA Markers**

J. H. M. Knoll, R. D. Nicholls, R. E. Magenis, K. Glatt, J. M. Graham Jr., L. Kaplan, and M. Lalonde 149

**Parental Origin of De Novo Constitutional Deletions of Chromosomal Band 11p13**

Vicki Huff, Anna Meadows, Vincent M. Riccardi, Louise C. Strong, and Grady F. Saunders 155

**A 6-bp Deletion 5' to the  $G\gamma$  Globin Gene in  $\beta^S$  Chromosomes Bearing the Bantu Haplotype**

Eric E. Bouhassira and Ronald L. Nagel 161

**Letters to the Editor**

**Population Screening for Cystic Fibrosis**

David Brock 164

**Risk Calculations under Heterogeneity:**

**Comment on a Letter by**

**D. E. Weeks and J. Ott**

Andrew D. Carothers 165

**Reply to Dr. Carothers: Support Intervals for Genetic Risks**

Daniel E. Weeks and Jurg Ott 166

**Association of Pigmentary Anomalies with Chromosomal and Genetic Mosaicism and Chimerism**

Andrew P. Read and Dian Donnai 166

**Reply to Read and Donnai**

I. T. Thomas and J. L. Frias 167

**Polymerase Chain Reaction-generated Heteroduplexes from Ashkenazi Tay-Sachs Carriers with an Insertion Mutation Can Be Detected on Agarose Gels**

Shirah Shore and Rachel Myerowitz 169

**Heteroduplex Formation in Polymerase Chain Reaction**

Franca Anglani, Luigi Picci, Cristina Camporese, and Franco Zacchello 169

**Book Review**

**New Developments in Biotechnology.** By the Office of Technology Assessment, Congress of the United States

Reviewed by Roger R. McFadden 171

**Errata** 172

**Announcements**

Employment and Fellowship Opportunities 173

## August 1990

## Editorial

**Invited Editorial: The Fragile X: Progress toward Solving the Puzzle**

W. Ted Brown

## Original Articles

**Microdissection of the Fragile X Region**

R. N. MacKinnon, M. C. Hirst, M. V. Bell, J. E. V. Watson, U. Claussen, H. J. Ludecke, G. Senger, B. Horsthemke, and K. E. Davies

175

**Physical Mapping of New DNA Probes near the Fragile X Mutation (FRAXA) by Using a Panel of Cell Lines**

G. K. Suthers, V. J. Hyland, D. F. Callen, I. Oberle, M. Rocchi, N. S. Thomas, C. P. Morris, C. E. Schwartz, M. Schmidt, H. H. Ropers, E. Baker, B. A. Oostra, N. Dahl, P. J. Wilson, J. J. Hopwood, and G. R. Sutherland

181

**Genetic Determination of Fragile-Site Expression**

Dominique Smeets and Ans Arets

196

**Mutations Causing Hemophilia B: Direct Estimate of the Underlying Rates of Spontaneous Germ-Line Transitions, Transversions, and Deletions in a Human Gene**

Dwight D. Koeberl, Cynthia D. K. Bottema, Rhett P. Ketterling, Peter J. Bridge, David P. Lillicrap, and Steve S. Sommer

202

**Sample-Size Guidelines for Linkage Analysis of a Dominant Locus for a Quantitative Trait by the Method of Lod Scores**

Michael Boehnke

218

**Friedreich Ataxia in Italian Families: Genetic Homogeneity and Linkage Disequilibrium with the Marker Loci D9S5 and D9S15**

Massimo Pandolfo, Giorgio Sirugo, Antonella Antonelli, Leonor Weitnauer, Luca Ferretti, Maurizio Leone, Ivano Dones, Antonella Cerino, Ricardo Fujita, Andre Hanauer, Jean-Louis Mandel, and Stefano Di Donato

228

**Molecular Definition of a Region of Chromosome 21 That Causes Features of the Down Syndrome Phenotype**

Julie R. Korenberg, Hiroko Kawashima, Stefan-M. Pulst, T. Ikeuchi, N. Ogasawara, K. Yamamoto, Steven A. Schonberg, Ruth West, Leland Allen, Ellen Magenis, K. Ikawa, N. Taniguchi, and Charles J. Epstein

236

**A Multivariate Method for Detecting Genetic Linkage, with Application to a Pedigree with an Adverse Lipoprotein Phenotype**

C. I. Amos, R. C. Elston, G. E. Bonney, B. J. B. Keats, and G. S. Berenson

247

**Joint Estimation of Recombination Fractions and Interference Coefficients in Multilocus Linkage Analysis**

Lue Ping Zhao, Elizabeth Thompson, and Ross Prentice

255

**Effective Testing of Gene-Disease Associations**

Michael Swift, Lawrence L. Kupper, and Charles L. Chase

266

**Gaucher Disease Type III (Norbottnian type) Is Caused by a Single Mutation in Exon 10 of the Glucocerebrosidase Gene**

Niklas Dahl, Maria Lagerström, Anders Erikson, and Ulf Pettersson

275

**Insertion of an Extra Codon for Threonine Is a Cause of Dihydropteridine Reductase Deficiency**

D. W. Howells, S. M. Forrest, H.-H. M. Dahl, and R. G. H. Cotton

279

**Pyruvate Dehydrogenase Deficiency Caused by Deletion of a 7-bp Repeat Sequence in the E1 $\alpha$  Gene**

H.-H. M. Dahl, C. Maragos, R. M. Brown, L. L. Hansen, and G. K. Brown

286

**Participation of Indo-European Tribes in Ethnogeny of the Mongoloid Population of Siberia: Analysis of the HLA Antigen Distribution in Mongoloids of Siberia**

V. V. Fefelova

294

## Minisymposium on Tyrosinemia

### Genetic Epidemiology of Hereditary Tyrosinemia in Quebec and in Saguenay-Lac-St-Jean

Marc De Braekeleer and Jean Larochelle 302

### Different Molecular Basis for Fumarylacetoacetate Hydrolase Deficiency in the Two Clinical Forms of Hereditary Tyrosinemia (type I)

R. M. Tanguay, J. P. Valet, A. Lescault, J. L. Duband, C. Laberge, F. Lettre, and M. Plante 308

### Visceral Pathology of Hereditary Tyrosinemia Type I

Pierre Russo and Sean O'Regan 317

### Fumarylacetoacetase Measurement as a Mass-screening Procedure for Hereditary Tyrosinemia Type I

Claude Laberge, André Grenier, J. P. Valet, and Jean Morissette 325

### Oral Loading of Homogentisic Acid in Controls and in Obligate Heterozygotes for Hereditary Tyrosinemia Type I

Claude Laberge, André Lescault, André Grenier, Jean Morissette, Richard Gagné, Pierre Gadbois, and John Halket 329

### Liver Transplantation for Hereditary Tyrosinemia: The Quebec Experience

Khazal Paradis, Andrée Weber, Ernest G. Seidman, Jean Larochelle, Laurent Garel, Catherine Lenaerts, and Claude C. Roy 338

## ASHG Committee Report and Membership Survey Results

### 1989 American Society of Human Genetics Social Issues Committee Report 343

### American Society of Human Genetics Membership Survey Results, 1989

Kenneth L. Garver and Kathleen M. Lent 345

## Letters to the Editor

### Sex Ratio among Sperm Cells

Renee H. Martin 349

### Progenitive Sex Ratio among Functioning Sperm Cells

Barry Bean 351

### The Patent of a Screening Test

James L. Waurin 353

### Reply to Waurin

Mark H. Bogart and O. W. Jones 353

### Worldwide Survey of the $\Delta F508$ Mutation—Report from the Cystic Fibrosis Genetic Analysis Consortium

The Cystic Fibrosis Genetic Analysis Consortium 354

### Carrier Screening for Cystic Fibrosis and Other Autosomal Recessive Diseases

Leo P. ten Kate 359

## Book Reviews

### *Tourette Syndrome and Human Behavior.* By

David E. Comings  
Reviewed by Susan E. Folstein 362

### *Tourette Syndrome and Human Behavior.* By

David E. Comings  
Reviewed by Arthur Robinson 363

### *The Politics of Woman's Biology.* By

Ruth Hubbard  
Reviewed by Florence P. Haseltine 364

### *The Biological Basis of Disease: Selected Papers by P. R. J. Burch.* Edited by M. S. Chesters and J. E. Burch

Reviewed by George M. Martin 364

## Announcements

Employment Opportunities; Conference, Meeting, and Symposium 366

## September 1990

## Original Articles

**The Molecular Basis of  $\beta$ -Thalassemia in Thailand: Application to Prenatal Diagnosis**

S. L. Thein, P. Winichagoon, C. Hesketh, S. Best,  
S. Fucharoen, P. Wasi, and D. J. Weatherall 369

**A Clinically Homogeneous Group of Families with Facioscapulohumeral (Landouzy-Déjérine) Muscular Dystrophy: Linkage Analysis of Six Autosomes**

Stephen J. Jacobsen, Edward S. Diala, Bruce V. Dorsey,  
Marcia B. Rising, Rebecca Graveline, Kathleen Falls,  
Paul Schultz, Christopher Hogan, Kenneth Rediker,  
Colette D'Amico, and Barbara Weiffenbach 376

**A Locus for Familial Hypertrophic Cardiomyopathy Is Closely Linked to the Cardiac Myosin Heavy Chain Genes, CRI-L436, and CRI-L329 on Chromosome 14 at q11-q12**

Scott D. Solomon, Anja A. T. Geisterfer-Lowrance,  
Hans-Peter Vosberg, Gudrun Hiller, John A. Jarcho,  
Cynthia C. Morton, Wesley O. McBride, Anna L. Mitchell,  
Allen E. Bale, William McKenna, J. G. Seidman,  
and Christine E. Seidman 389

**Genetic Mapping of Two New DNA Markers in Xq26-Xq28 Relative to the Fragile-X Syndrome Locus**

R. Sood, L. M. Mulligan, R. Poon, B. N. White,  
and J. J. A. Holden 395

 **$\alpha$ 1-Antitrypsin Nullisoma di procida: An  $\alpha$ 1-Antitrypsin Deficiency Allele Caused by Deletion of All  $\alpha$ 1-Antitrypsin Coding Exons**

H. Takahashi and R. G. Crystal 403

**Genetic Analysis of Apolipoprotein A-I in Two Dietary Environments**

John Blangero, Jean W. MacCluer, Candace M. Kammerer,  
Glen E. Mott, Thomas D. Dyer,  
and Henry C. McGill, Jr. 414

**Variation at the Apolipoprotein (apo) A1-CIII-AIV Gene Cluster and Apo B Gene Loci Is Associated with Lipoprotein and Apolipoprotein Levels in Italian Children**

C.-F. Xu, M. N. Nanjee, J. Savill, P. J. Talmud, F. Angelico,  
M. Del Ben, R. Antonini, B. Mazzarella, N. Miller,  
and S. E. Humphries 429

**Identification of the Base-Pair Substitution Responsible for a Human Acid Alpha Glucosidase Allele with Lower "Affinity" for Glycogen (GAA 2) and Transient Gene Expression in Deficient Cells**

F. Martiniuk, M. Bodkin, S. Tzall, and R. Hirschhorn 440

**Allan-Herndon Syndrome. I. Clinical Studies**

Roger E. Stevenson, Harold O. Goodman,  
Charles E. Schwartz, Richard J. Simensen,  
William T. McLean, Jr., and C. Nash Herndon 446

**Allan-Herndon Syndrome. II. Linkage to DNA Markers in Xq21**

Charles E. Schwartz, Joan Ulmer, Angela Brown,  
Ian Pancoast, Harold O. Goodman,  
and Roger E. Stevenson 454

**Human Chromosome 5 Complements the DNA Double-Strand Break-Repair Deficiency and Gamma-Ray Sensitivity of the XR-I Hamster Variant**

A. J. Giaccia, N. Denko, R. MacLaren, D. Mirman,  
C. Waldren, I. Hart, and T. D. Stamato 459

**Monte Carlo Comparison of Preliminary Methods for Ordering Multiple Genetic Loci**

Jane M. Olson and Michael Boehnke 470

**Genes for Two Autosomal Recessive Forms of Chronic Granulomatous Disease Assigned to 1q25 (NCF2) and 7q11.23 (NCF1)**

Uta Francke, Chih-Lin Hsieh, Brigitte E. Foellmer,  
Karen J. Lomax, Harry L. Malech, and Thomas L. Leto 483

**The Isochromosome 18p Syndrome: Confirmation of Cytogenetic Diagnosis in Nine Cases by In Situ Hybridization**

D. F. Callen, C. J. Freemantle, M. L. Ringenbergs, E. Baker,  
H. J. Eyre, D. Romain, and E. A. Haan 493

**Application of DNA Fingerprints for Cell-Line Individualization**

Dennis A. Gilbert, Yvonne A. Reid, Mitchell H. Gail,  
David Pee, Christine White, Robert J. Hay,  
and Stephen J. O'Brien 499

**HLA-DQ $\alpha$  Allele and Genotype Frequencies in Various Human Populations Determined by Using Enzymatic Amplification and Oligonucleotide Probes**

Rhea Helmuth, Nicola Fildes, Edward Blake, Michael C. Luce, J. Chimera, Roberta Madej, C. Gorodezky, Mark Stoneking, Norma Schmill, William Klitz, Russell Higuchi, and Henry A. Erlich

515

**Exclusion of a Schizophrenia Susceptibility Gene from the Chromosome 5q11-q13 Region: New Data and a Reanalysis of Previous Reports**

Peter McGuffin, Matthew Sargeant, Gillian Hett, Simon Tidmarsh, Stephen Whatley, and R. M. Marchbanks

524

**Linkage to D3S47 (C17) in One Large Autosomal Dominant Retinitis Pigmentosa Family and Exclusion in Another: Confirmation of Genetic Heterogeneity**

D. H. Lester, C. F. Inglehearn, R. Bashir, H. Ackford, L. Esakowitz, M. Jay, A. C. Bird, A. F. Wright, S. S. Papiha, and S. S. Bhattacharya

536

**Combined Segregation and Linkage Analysis of Genetic Hemochromatosis Using Affection Status, Serum Iron, and HLA**

I. B. Borecki, G. M. Lathrop, G. E. Bonney, J. Yaouanq, and D. C. Rao

542

**Synaptophysin: Structure of the Human Gene and Assignment to the X Chromosome in Man and Mouse**

Tayfun Özçelik, Ronald G. Lafreniere, Branch T. Archer III, Patricia A. Johnston, Huntington F. Willard, Uta Francke, and Thomas C. Südhof

551

**Hereditary Fructose Intolerance Caused by a Nonsense Mutation of Aldolase B Gene**

Susumu Kajihara, Tsunehiro Mukai, Yuji Arai, Misao Owada, Teruo Kitagawa, and Katsuji Hori

562

**A New Point Mutation in  $\beta$ -Hexosaminidase  $\alpha$  Subunit Gene Responsible for Infantile Tay-Sachs Disease in a Non-Jewish Caucasian Patient (a *Kpn* Mutant)**

Akemi Tanaka, Hope H. Punnett, and Kunihiko Suzuki

568

**Molecular Genetics of the Glucose-6-Phosphate Dehydrogenase (G6PD) Mediterranean Variant and Description of a New G6PD Mutant, G6PD Andalus<sup>1361A</sup>**

J.-L. Vives-Corrons, W. Kuhl, M. A. Pujades, and E. Beutler

575

**Letters to the Editor**

**The Ethics of Cystic Fibrosis Carrier Screening: Where Do We Stand?**

Marc De Braekeleer and Marcel J. Mélançon

580

**Gestational Age at Maternal Serum Alpha-Fetoprotein Screening and the Detection of Down Syndrome**

Kim Waller, Linda Lustig, and Ernest Hook

581

**Reply to Waller et al.**

Frank Greenberg, Deborah Del Junco, and Elliot Alpert

583

**Defining DNA Diagnostic Tests Appropriate for Standard Clinical Care**

Roger V. Lebo, George Cunningham, Malcolm J. Simons, and Larry J. Shapiro

583

**Appendectomy in Australian Twins**

David L. Duffy, Nicholas G. Martin, and John D. Mathews

590

**A Likelihood-based Analysis of Consistent Linkage of a Disease Locus to Two Nonsyntenic Marker Loci: Osteogenesis Imperfecta versus COL1A1 and COL1A2**

Daniel E. Weeks

592

**Reply to Weeks**

Bryan Sykes

593

**Book Reviews**

**Turner Syndrome.** Edited by Ron G. Rosenfeld and Melvin M. Grumbach

Reviewed by Göran Annerén

595

**Myotonic Dystrophy, 2d ed.** By Peter S. Harper

Reviewed by Allen D. Roses

596



- Genetic Strains and Variants of the Laboratory Mouse, 2d ed.** Edited by M. F. Lyon and A. G. Searle  
Reviewed by Greg Barsh 596

Erratum 598

## Announcements

- Employment and Fellowship Opportunities;  
Conference 599

## October 1990

### Editorials

- Editorial: Making History**  
Charles J. Epstein, Editor

- Invited Editorial: Carrier Screening for Cystic Fibrosis**  
Arthur L. Beaudet

### Original Articles

- Cystic Fibrosis Mutations in North American Populations of French Ancestry: Analysis of Quebec French-Canadian and Louisiana Acadian Families**

Rima Rozen, Robert H. Schwartz, Bettina C. Hilman, Pat Stanislovitis, Glenn T. Horn, Katherine Klinger, Jocelyne Daigneault, Marc De Braekeleer, Bat-sheva Kerem, Lap-Chee Tsui, T. Mary Fujiwara, and Kenneth Morgan

- Benign Missense Variations in the Cystic Fibrosis Gene**

Keiko Kobayashi, Michael R. Knowles, Richard C. Boucher, William E. O'Brien, and Arthur L. Beaudet

- Linkage Relationship of X-linked Juvenile Retinoschisis with Xp22.1-p22.3 Probes**

Paul A. Sieving, Eve L. Bingham, Mark S. Roth, Martin R. Young, Michael Boehnke, Chen-Yu Kuo, and David Ginsburg

- Deletions in Patients with Classical Choroideremia Vary in Size from 45 kb to Several Megabases**

601 Frans P. M. Cremers, Eeva-Marja Sankila, Frank Brunsmann, Marcelle Jay, Barrie Jay, Alan Wright, Alfred J. L. G. Pinckers, Marianne Schwartz, Dorien J. R. van de Fol, Bé Wieringa, Albert de la Chapelle, Ivar H. Pawlowitzki, and Hans-Hilger Ropers 622

- An Example of Leber Hereditary Optic Neuropathy Not Involving a Mutation in the Mitochondrial ND4 Gene**

Neil Howell and David McCullough 629

- Genetics and Biology of Human Ovarian Teratomas. I. Cytogenetic Analysis and Mechanism of Origin**

Urvashi Surti, Lori Hoffner, Aravinda Chakravarti, and Robert E. Ferrell 635

- Genetics and Biology of Human Ovarian Teratomas. II. Molecular Analysis of Origin of Nondisjunction and Gene-Centromere Mapping of Chromosome 1 Markers**

606 Ranjan Deka, Aravinda Chakravarti, Urvashi Surti, Ellyn Hauselman, Jillian Reefer, Partha P. Majumder, and Robert E. Ferrell 644

- Cytogenetic Analysis of 750 Spontaneous Abortions with the Direct-Preparation Method of Chorionic Villi and Its Implications for Studying Genetic Causes of Pregnancy Wastage**

611 Bernd Eiben, Iris Bartels, Susan Bähr-Porsch, Sabine Borgmann, Gudrun Gatz, Gaby Gellert, Richard Goebel, Wilhelm Hammans, Martha Hentemann, Rüdiger Osmers, Rüdiger Rauskolb, and Ingo Hansmann 656

**Definitive Localization of X-linked Kallman Syndrome (Hypogonadotropic Hypogonadism and Anosmia) to Xp22.3: Close Linkage to the Hypervariable Repeat Sequence CRI-S232**

T. Meitinger, B. Heye, C. Petit, J. Leveilliers, A. Golla, C. Moraine, B. Dalla Piccola, W. G. Sippell, J. Murken, and A. Ballabio

664

**Phenotypic Heterogeneity in Osteogenesis Imperfecta: The Mildly Affected Mother of a Proband with a Lethal Variant Has the Same Mutation Substituting Cysteine for  $\alpha$ 1-Glycine 904 in a Type I Procollagen Gene (COL1A1)**

Constantinos D. Constantinou, Michael Pack, Sheila B. Young, and Darwin J. Prockop

670

**Assignment of the Charcot-Marie-Tooth Neuropathy Type I (CMT 1a) Gene to 17p11.2-p12**

Vincent Timmerman, Peter Raeymaekers, Peter De Jonghe, Goedele De Winter, Lorry Swerts, Karel Jacobs, Jan Gheuens, Jean-Jacques Martin, Antoon Vandenbergh, and Christine Van Broeckhoven

680

**Alleles at the PRB3 Locus Coding for a Disulfide-bonded Human Salivary Proline-rich Glycoprotein (GI 8) and a Null in an Ashkenazi Jew**

E. A. Azen, K. Minaguchi, P. Latreille, and H.-S. Kim

686

**Frequency of Three Hex A Mutant Alleles among Jewish and Non-Jewish Carriers Identified in a Tay-Sachs Screening Program**

Barry H. Paw, Phuong T. Tieu, Michael M. Kaback, Joyce Lim, and Elizabeth F. Neufeld

698

**DNA Haplotype Analyses of Patients with Hyperphenylalaninemia**

Deborah Di Silvestre, Arti Pandya, Richard Koch, and John Groffen

706

**Haplotype Analysis of the Human Apolipoprotein B Mutation Associated with Familial Defective Apolipoprotein B100**

Erwin H. Ludwig and Brian J. McCarthy

712

**Compound Heterozygote for Lipoprotein Lipase Deficiency: Ser $\rightarrow$ Thr<sup>244</sup> and Transition in 3' Splice Site on Intron 2 (AG $\rightarrow$ AA) in the Lipoprotein Lipase Gene**

Akira Hata, Mitsuru Emi, Gerald Luc, Alain Basdevant, Philippe Gambert, Per-Henrik Iverius, and Jean-Marc Lalouel

721

**Thyroid Antibodies as a Risk Factor for Down Syndrome and Other Trisomies**

C. P. Torfs, B. J. van den Berg, F. W. Oechsli, and R. E. Christianson

727

**Definitive Prenatal Diagnosis for Type III Glycogen Storage Disease**

Bing-Zhi Yang, Jia-Huan Ding, Barbara I. Brown, and Yuan-Tsong Chen

735

**Letters to the Editor**

**Screening for Cystic Fibrosis Carriers**

Joseph D. Schulman, Anne Maddalena, Susan H. Black, and David P. Bick

740

**Regarding Criticism on Update of MSAFP Policy Statement from the ASHG**

Mark R. Geier and John L. Young

740

**Some Issues in the Study of Birth Defects and Recurrence Risks in Live Births and "Stillbirths"**

Ernest B. Hook

741

**Reply to Dr. Hook**

Sonja Rasmussen, Joseph Mulinare, and Muin J. Khoury

742

**Identical Point Mutations in the Factor VIII Gene That Have Different Clinical Manifestations of Hemophilia A**

R. Schwaab, M. Ludwig, J. Oldenburg, H. H. Brackmann, H. Egli, L. Kochhan, and K. Olek

743

**Book Reviews**

**Environmental Causes of Human Birth Defects.**

By T. V. N. Persaud

Reviewed by Mason Barr, Jr.

745



**On Stress, Disease and Evolution.**

By Graham W. Boyd

Reviewed by Frederick Hecht and Barbara K. Hecht 745

**Human Genetics Education Section****Editorial: Integrating Genetics into the Medical School Curriculum**

Carl A. Huether 748

**Letter to the Editor: Physicians and Other Nongeneticists Strongly Favor Teaching Genetics to Medical Students in United Kingdom Survey**

Rodney Harris 750

**Innovations in Human Genetics Education: Incorporation of Genetics into a Problem-based Medical School Curriculum**

Ann E. Swinford and Douglas B. McKeag 753

**Educational Resources: Book Reviews****Genetics: Human Aspects.** By Arthur P. Mange and Elaine J. Mange

Reviewed by Margretta R. Seashore 759

**Pictorial Human Embryology.** By Stephen G. Gilbert

Reviewed by Lawrence G. Erway 760

**Principles of Population Genetics. 2d ed.**

By Daniel E. Hartl and Andrew G. Clark

Reviewed by Peter E. Smouse 761

**Principles of Genetics, 2d ed.** By James W. Frstrom and Michael T. Clegg**Genetics, 2d ed.** By Peter J. Russell  
Reviewed by Emanuel Hackel 762**Genes and Gender I.** Edited by Ethel Tobach and Betty Rosoff**Genes and Gender II: Pitfalls in Research on Sex and Gender.** Edited by Ruth Hubbard and Marian Lowe**Genes and Gender III: Genetic Determinism and Children.** Edited by Ethel Tobach and Betty Rosoff**Genes and Gender IV: The Second X and Women's Health.** Edited by Myra Fodden, Susan Gordon, and Betty Hughley**Genes and Gender V: Socialization toward Inequity.** Edited by Georgine Vroman, Dorothy Burnham, and Susan Gordon**Genes and Gender VI: The Gendered Face of Peace and War: A Challenge to Genetic Determinism.** Edited by Betty Rosoff and Ethel Tobach

Reviewed by Robert C. Baumiller 763

**Announcements**Employment and Fellowship Opportunities;  
Conference; Call for Patients 764**November 1990****Original Articles****Alkaline Phosphatase (tissue nonspecific isoenzyme) Is a Phosphoethanolamine and Pyridoxal-5'-Phosphate Ectophosphatase: Normal and Hypophosphatasia Fibroblast Study**

Kenton N. Fedde and Michael P. Whyte 767

**Pseudohypophosphatasia: Aberrant Localization and Substrate Specificity of Alkaline Phosphatase in Cultured Skin Fibroblasts**

Kenton N. Fedde, D. E. C. Cole, and Michael P. Whyte 776

**Identification of Point Mutations in the  $\alpha$ -Galactosidase A Gene in Classical and Atypical Hemizygotes with Fabry Disease**

Hitoshi Sakuraba, Akihiro Oshima, Yukiko Fukuhara, Michie Shimamoto, Yoshiro Nagao, David F. Bishop, Robert J. Desnick, and Yoshiyuki Suzuki 784

**Splicing Defect at the Ornithine Aminotransferase (OAT) Locus in Gyrate Atrophy**

Andrea I. McClatchey, Daniel L. Kaufman, Eliot L. Berson, Allan J. Tobin, Vivian E. Shih, James F. Gusella, and Vijaya Ramesh 790

**Deletion Mapping of Åhland Island Eye Disease to Xp21 between DXS67 (B24) and Duchenne Muscular Dystrophy**

De-Ann M. Pillers, Jeffrey A. Towbin, Jeffrey S. Chamberlain, Darong Wu, Joel Ranier, Berkeley R. Powell, and Edward R. B. McCabe 795

**Chromosomal Localization of the Human  $\alpha$ -L-Iduronidase Gene (*IDUA*) to 4p16.3**

Hamish S. Scott, Lesley J. Ashton, Helen J. Eyre, Elizabeth Baker, Doug A. Brooks, David F. Callen, Grant R. Sutherland, C. Phillip Morris, and John J. Hopwood 802

**Heterozygous Mutations at the *mut* Locus in Fibroblasts with *mut*<sup>o</sup> Methylmalonic Acidemia Identified by Polymerase-Chain-Reaction cDNA Cloning**

Ruud Jansen and Fred D. Ledley 808

**More Than One Mutant Allele Causes Infantile Tay-Sachs Disease in French-Canadians**

Peter Hechtman, Feige Kaplan, Janet Bayleran, Bernard Boulay, Eva Andermann, Marc de Braekeleer, Serge Melançon, Marie Lambert, Michael Potier, Richard Gagné, Edwin Kolodny, Carol Clow, Aniceta Capua, Claude Prevost, and Charles Scriver 815

**Equal Parental Origin of Chromosome 22 Losses in Human Sporadic Meningioma: No Evidence for Genomic Imprinting**

Bertrand Fontaine, Guy A. Rouleau, Bernd R. Seizinger, Ann F. Jewell, Mark P. Hanson, Robert L. Martuza, and James F. Gusella 823

**A Human D<sub>1</sub> Dopamine Receptor Gene Is Located on Chromosome 5 at q35.1 and Identifies an *EcoRI* RFLP**

David K. Grandy, Qun-Yong Zhou, Lee Allen, Ruth Litt, R. Ellen Magenis, Olivier Civelli, and Michael Litt 828

**The Pattern of Factor IX Germ-Line Mutation in Asians Is Similar to That of Caucasians**

Cynthia D. K. Bottema, Rhett P. Ketterling, Hong-Sup Yoon, and Steve S. Sommer 835

**The Probabilistic Determination of Identity-by-Descent Sharing for Pairs of Relatives from Pedigrees**

C. I. Amos, D. V. Dawson, and R. C. Elston 842

**Minisatellite Allele Diversification: The Origin of Rare Alleles at the *HRAS1* Locus**

Andreas Kasperczyk, Nancy A. DiMartino, and Theodore G. Krontiris 854

**Further Mapping of an Ataxia-Telangiectasia Locus to the Chromosome 11q23 Region**

O. Sanal, S. Wei, T. Foroud, U. Malhotra, P. Concannon, P. Charmley, W. Salser, K. Lange, and R. A. Gatti 860

**Diversity of Some Gene Frequencies in European and Asian Populations. V. Steep Multilocus Clines**

Guido Barbujani, Geoffrey M. Jacquez, and Laura Ligi 867

**Letters to the Editor**

**DNA Typing in the Forensic Arena**

Paul J. Hagerman 876

**Parental Origin of Chromosome 22 Alleles Lost in Meningioma**

M. Sanson, O. Delattre, J. Couturier, J. Philippon, J. Cophignon, P. Derome, G. A. Rouleau, and G. Thomas 877

**Hexosaminidase—Pseudodeficiency?**

Joachim Kappler, Volkmar Gieselmann, and Peter Propping 880

**Reply to Kappler et al.**

Richard L. Proia, Edwin H. Kolodny, and Ruth Navon 881

**Erratum**

883

**Announcements**

**Employment and Fellowship Opportunities; Menkes Disease Treatment Protocol; International Exchange; Course**

884

## December 1990

## Allen Award Addresses

**1989 Allen Award Address: The American Society of Human Genetics Annual Meeting, Baltimore**

David Botstein

887

**1989 Allen Award Address: The American Society of Human Genetics Annual Meeting, Baltimore**

Ray White

892

## Editorial

**Invited Editorial: State-sponsored Maternal Serum Alpha-Fetoprotein Activities: Current Issues in Genetics and Public Health**

Jessica G. Davis

896

## Genetics and Public Health

**Maternal Serum Alpha-Fetoprotein Screening Activities of State Health Agencies: A Survey**

George C. Cunningham and Kenneth W. Kizer

899

## Original Articles

**Nucleus-driven Multiple Large-Scale Deletions of the Human Mitochondrial Genome: A New Autosomal Dominant Disease**

Massimo Zeviani, Nereo Bresolin, Cinzia Gellera, Andreina Bordon, Marilou Pannacci, Patrizia Amati, Maurizio Moggi, Serenella Servidei, Guglielmo Scarlato, and Stefano Di Donato

904

**Genetic Linkage and Heterogeneity in Type I Charcot-Marie-Tooth Disease (Hereditary Motor and Sensory Neuropathy Type I)**

Phillip F. Chance, Thomas D. Bird, Peter O'Connell, Hillary Lipe, Jean-Marc Lalouel, and Mark Leppert

915

**Isolation of a Marker Linked to the Charcot-Marie-Tooth Disease Type 1A Gene by Differential *Alu*-PCR of Human Chromosome 17-retaining Hybrids**

Pragna I. Patel, Carlos Garcia, Roberto Montes de Oca-Luna, Richard I. Malamut, Brunella Franco, Susan Slaugenhaupt, Aravinda Chakravarti, and James R. Lupski

926

**Localization of the Microsatellite Probe DXS426 between DXS7 and DXS255 on Xp and Linkage to X-linked Retinitis Pigmentosa**

Michael Coleman, Shomi Bhattacharya, Susan Lindsay, Alan Wright, Marcelle Jay, Michael Litt, Ian Craig, and Kay Davies

935

**Autosomal Dominant Retinitis Pigmentosa: Absence of the Rhodopsin Proline→Histidine Substitution (Codon 23) in Pedigrees from Europe**

G. J. Farrar, P. Kenna, R. Redmond, P. McWilliam, D. G. Bradley, M. M. Humphries, E. M. Sharp, C. F. Inglehearn, R. Bashir, M. Jay, A. Watty, M. Ludwig, A. Schinzel, C. Samanns, A. Gal, S. Bhattacharya, and P. Humphries

941

**The Mutation for Medullary Thyroid Carcinoma with Parathyroid Tumors (MTC with PTs) Is Closely Linked to the Centromeric Region of Chromosome 10**

Nancy L. Carson, Jingshi Wu, Charles E. Jackson, Kenneth K. Kidd, and Nancy E. Simpson

946

**A New DNA Marker (D10S94) Very Tightly Linked to the Multiple Endocrine Neoplasia Type 2A Locus (MEN2A) Locus**

Paul J. Goodfellow, Shirley Myers, Linda L. Anderson, Angela R. Brooks-Wilson, and Nancy E. Simpson

952

**Multipoint Analysis of Human Quantitative Genetic Variation**

David E. Goldgar

957

**Analysis of DNA Polymorphisms Suggests That Most De Novo dup(21q) Chromosomes in Patients with Down Syndrome Are Isochromosomes and Not Translocations**

Stylianos E. Antonarakis, Patricia A. Adelsberger, Michael B. Petersen, Franz Binkert, and Albert A. Schinzel 968

**Localization of the Human Angiogenin Gene to Chromosome Band 14q11, Proximal to the T Cell Receptor  $\alpha/\delta$  Locus**

Stanisława Weremowicz, Edward A. Fox, Cynthia C. Morton, and Bert L. Vallee 973

**Genetic Linkage Map of Six Polymorphic DNA Markers around the Gene for Familial Adenomatous Polyposis on Chromosome 5**

M. G. Dunlop, A. H. Wyllie, Y. Nakamura, C. M. Steel, H. J. Evans, R. L. White, and C. C. Bird 982

**Replication Patterns of the Fragile X in Heterozygous Carriers: Analysis by a BrdUrd Antibody Method**

Hirofumi Ohashi, Akira Kuwano, Masato Tsukahara, Tadao Arinami, and Tadashi Kajii 988

**The Human CYP2D Locus Associated with a Common Genetic Defect in Drug Oxidation: A G1934→A Base Change in Intron 3 of a Mutant CYP2D6 Allele Results in an Aberrant 3' Splice Recognition Site**

Nobumitsu Hanioka, Shiko Kimura, Urs A. Meyer, and Frank J. Gonzalez 994

**A Termination Mutation Prevalent in Norwegian Haplotype 7 Phenylketonuria Genes**

J. Apold, H. G. Eiken, E. Odland, Å. Fredriksen, A. Bakken, J. B. Lorens, and H. Boman 1002

**The NT 1311 Polymorphism of G6PD: G6PD Mediterranean Mutation May Have Originated Independently in Europe and Asia**

Ernest Beutler and Wanda Kuhl 1008

**Origin and Spread of the Glucose-6-Phosphate Dehydrogenase Variant (G6PD Mediterranean) in the Middle East**

Buran Kurdi-Haidar, Philip John Mason, Alain Berrebi, George Ankra-Badu, Amin Al-Ali, Ariella Oppenheim, and Lucio Luzzatto 1013

**Recombination between Two 14-bp Homologous Sequences as the Mechanism for Gene Deletion in Factor IX<sub>Seattle</sub> 1**

Shi-Han Chen and C. Ronald Scott 1020

## Letters to the Editor

**Rapid Detection of the Hemoglobin C Mutation by Allele-specific Polymerase Chain Reaction**

Nathan Fischel-Ghodsian, Phyllis C. Hirsch, and Marlene C. Bohlman 1023

**The Slash Sheet: A Simple Procedure for Risk Analysis in Cystic Fibrosis**

J. H. Edwards and A. Miciak 1024

**Re: Book Review of New Developments in Biotechnology**

Roger C. Herdman 1028

**Family Cell Lines Available for Research**

Åke Lernmark, Lee Ducat, George Eisenbarth, Jurg Ott, M. Alan Permutt, Pablo Rubinstein, and Richard Spielman 1028

## Book Review

**Progress in Clinical and Biological Research, vol. 329: Multipoint Mapping and Linkage Analysis Based upon Affected Pedigree Members: Genetic Analysis Workshop 6.**

Edited by R. C. Elston, M. A. Spence, S. E. Hodge, and J. W. MacCluer  
Reviewed by Michael Boehnke 1031

## Announcements

**Employment and Fellowship Opportunities; Cytogenetic Nomenclature Standards; Conference and Symposium** 1033

**1990 Diplomates of The American Board of Medical Genetics** 1035

**Editorial Reviewers** 1039

**Author Index to Volume 47** 1043

**Subject Index to Volume 47** 1048

**Contents of Volume 47** 1059

